The Importance of Clinical Research in the Care of the Patient

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THE reason for presenting this Symposium on Clinical Research is to provide an opportunity to discuss the immediate necessity and great importance of expanding in Canada our potential for the scientific study of patients in order to improve the care which can be provided for them. As physicians, our primary challenge and objective is to heal the sick, and the rates of the various developments within our increasingly complex *modus operandi* must be reviewed recurrently in the light of this traditional objective. As expressed recently by Burnet,[1] "the aim of medicine in the broadest sense is to provide for every human being, from conception to death, the greatest fullness and length of life that is allowed by his genetic constitution and by the accidents of life". To this end the science of medicine and the art of healing go hand in hand to complement each other, and it is our moral responsibility as physicians to keep both facets properly balanced.

The term "clinical research" is relatively new and often confusing, but the principle involved is as old as the history of medicine. To gain a clearer insight into the role of scientific investigation in the care of the patient, some backward glances will highlight some of these developments. In the evolution from the prehistoric practices of the tribal medicine man, down through the early times when physicians began to search for rhyme and reason in the ills of their patients, a continuing effort to systematize knowledge, soundly based on observation and experiment, has been the keystone in increasing success in the healing of the sick. For instance, as far back as the age of Hindu medicine practised in the era 800-600 B.C., the disease, diabetes mellitus, was identified by the name "honey urine", since it was noted that trains of black ants were attracted to the sweet urine and provided a means of diagnosis.[2]

Later the Greeks, in the fifth to third centuries B.C., championed the scientific spirit as embodied in the art of medicine taught by Hippocrates. The trend was continued by Aristotle, who clearly recognized the fundamental problems of biology, sex, heredity, nutrition, growth and adaptation.[3]

Following the decline of western medicine during the "dark ages", the Renaissance period emerged in the fifteenth century and witnessed the rise again of scientific endeavour which has continued to have an increasing impact on the practice of medicine ever since. The rise of anatomy, physiology and chemistry was closely entwined with the practice of medicine at this period and the wealth of information gradually increased in these main streams of scientific endeavour. However, the body of knowledge was sufficiently small so that the giants of the day encompassed much learning in many fields. An example was Francis Glisson, Regius Professor of Medicine at Cambridge in 1636, who was described at once as a philosopher, anatomist, physiologist, pathologist, orthopedic surgeon and clinician.[3]

The highly acceptable attitude of scientific enquiry and observation characteristic of the Renaissance brought forth works of tremendous importance in medicine, the clinical research of that period: proof of the circulation of the blood by Harvey, advances in surgical techniques by Paré and descriptions of anatomy by Vesalius, to mention only a few.

One stamp of the scientific renaissance imprinted on England was the action aroused by Thomas Linacre, who, alarmed that the healing of the sick was left in the hands of a great host of quacks, charlatans and impostors, established the Royal College of Physicians of London in 1518. The consequent limitation of the practice of medicine to properly trained and licensed scholars has set a pattern which has ensured a profession of dedicated men and women since that time.

To this day, the training of the physician is based upon these principles established down through the centuries. He is trained primarily in the science of medicine; firstly the basic sciences of chemistry, physiology and anatomy and later at the bedside as these apply to the healing of the sick.

The increasing growth of scientific endeavour, overlapping so closely the field of medicine, continued to attract men with intellectual curiosity troubled by their inadequacy to combat disease in their patients as well as in animals. The strides being made by the mid-nineteenth century were reflected by the accomplishments of Koch in the field of tuberculosis and Pasteur in the control of infectious diseases.

Following this the conviction arose that furthering the advance of medical scientific knowledge for the care of the sick required an endeavour greater than that provided by the universities and medical schools at that time. This conviction found expression through the development of institutions for special research, oriented to those recent accomplishments in preventive medicine. In Europe much progress was made in the fields of bacteri-

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ology and immunity in the Koch Institute, the Pasteur Institute and the Lister Institute.

By the turn of the century a further stage of development was initiated. On the American scene, the Rockefeller Institute transformed the concept of medical research in that it became the first institute to be established for the development of fundamental research without any restriction on its field of activity, the laboratories being located in juxtaposition to the hospital beds, for the study in depth of patients with a variety of diseases. Frederick J. Gates, the Baptist minister, who as adviser to John D. Rockefeller, Jr., had conceived the idea, revealed amazing wisdom and foresight when he suggested that "medicine can hardly hope to become a science until it can be endowed, and qualified men enabled to give themselves to uninterrupted study and investigation, on ample salary, entirely independent of practice".[4]

The early developmental work on the blood groups by Landsteiner, the great advances in biochemical technology contributed by Van Slyke and delineations on the abnormalities of blood proteins by Dr. Kunkel, who is with us today, reflect only a few of the results of clinical research carried out at this Institute. The impact of this Institute and of Simon Flexner upon medical education in America in the early part of this century was comparable to the changes wrought by Linacre in England three hundred years earlier.

Thus with the increasing tempo in all fields of scientific endeavour which has occurred in the past half century, physicians in the academic centres are addressing themselves increasingly to scientific analysis of unresolved patterns of disease in their patients. As a result of this increasing tendency to bring the scientific method to the bedside, better medicine is being taught and practised. Learned societies, such as our Canadian Society for Clinical Investigation, have sprung up, at which the medical investigators meet regularly to communicate their new-found knowledge and to withstand the leavening discipline of criticism from their fellows.

The effect of this continuing scientific evolution in medicine has been the development of specialty services, the body of knowledge in any one field and the resultant skills of application to the care of patients being so great that a man can reasonably hope to master in depth only one area. What a contrast to the broad orientation descriptive of Robert Glisson in 1636!

What is the future of this trend? Pondering this question recently, Sir Russell Brain suggested that medicine is entering into a new dimension.[5] The basic knowledge and skills are not as unitarian as they once seemed. We draw from anatomy, biochemistry, physiology, pharmacology, and psychology in synthesizing our understandings of, for instance, disorders of the nervous system. Organs and organ functions are being replaced by what Brain refers to as biological transactions. Recent research has been concerned with knowledge of the smallest biological units which take part in transactions at the molecular level, the chemistry of hormones, the transfer of chemical information from generation to generation by genes, and so forth. The fundamental principles of medicine which will apply to the care of the patient will increasingly be reoriented to knowledge of such basic biological transactions organized at increasing levels of complexity.

It is apparent that the role of a clinical investigator falls somewhere between the basic medical scientist, the biochemist or physiologist, and the physician trained and skilled primarily in the treatment of the sick.

From the patient's point of view, what is the difference between a basic scientist and a clinical scientist to whom he looks for mental and physical care? Both are concerned with the acquisition of new knowledge in the field of medical biology; both use the same types of laboratory procedures and methods of analysis; both may study biological behaviour in animals because of the similarity to the biological mechanisms in man. The only difference is that the clinical investigator who is trained as a physician applies the results of his investigation directly to the benefit of the patient and others like him. As Tanner[6] has suggested recently in defining a physician, he is in fact an applied human biologist. The basic medical scientist, although working at no more fundamental level, is carrying out biological studies not necessarily involving patient care, but which may have more or less direct application in clinical medicine.

Since the problems arise from the sick patient, the investigation of these problems must go on largely in a hospital environment. The clinical investigator therefore fills a dual role in bringing the elements of the basic science to the bedside with the physician and provides a bridge of communication between these two important areas of scientific enquiry.

Concern has been expressed lest the cold logic of scientific inquiry which must be inculcated in an investigator interfere with the sensitive humanistic attitude he should, as a physician, express to the patient. For the sincere understanding man no such problem exists. As a physician, his sensitive appreciation of the patient's plight ranks uppermost, and his scientific knowledge is truly effective only when humanely and humbly directed. Thus the spirit of scientific medicine can fuse naturally and beneficially with the art of medicine in the care of the sick.[7]

Against this background, are we in Canada keeping pace with the progress of scientific medicine so important in improving the standard of health of our people?

There is no question that we are not. The specific areas and problems will be spelled out in the other

contributions to this symposium. Certainly our present economy and standard of living permit a reorientation of legislative policy in this regard.

It must be clearly recognized that considerable efforts to change this program have already been made, and much credit must go to our responsible medical and lay leaders. The increased financial support, both federal and private, in recent years has made its impact to a greater or lesser extent in all medical schools through increased programs of grants for research and construction. The growth of the Canadian Society for Clinical Investigation is an excellent reflection of this trend.

The story of the past which I have outlined leaves no doubt of the certain promise for the future accomplishment of medicine. The members of this Society feel most emphatically that for patient care to be of increasing superiority, it is vital that the people of Canada understand the situation and demand that increasing investment be made in scientific medicine in order to provide that care.

We have a challenge for leadership not only at home, but internationally as well.

Assured of continuance of the highest standards of moral responsibility and humanistic attitude for which the physician strives, the patient must surely welcome the increasing benefits which accrue to him from the broadening scope of clinical research.

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The Basic Scientist in the University Hospital

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IN order to discuss the problem of integration of the "basic scientist" into the University Hospital, I must first sketch very briefly the features of the contemporary scene in clinical investigation which bear upon this relationship. We must recognize three major factors.

1. Medicine, like biology, has an urgent need of the help of pure chemists, biophysicists, etc. This need exists throughout the biological field and does not indicate any inherent "weakness" in clinical research. In this context I would like to quote the following passage from the *Bulletin* of the American Institute of Biological Sciences (October 1961, page 31): "The Harvard Department of Biology is putting into effect a major revision in its plan for the undergraduate study of biology. This change is in recognition of rapid developments in the science of biology and the need to utilize the tools of chemistry, physics and mathematics in certain types of biological research." Unless clinical research is to be limited to clinical therapeutic trials and clinical observation, it necessarily involves the full exploitation of new tools—and historically it has always involved this. It is essential to distinguish between clinical observation and clinical research and experimentation, and one might refer the reader to the papers of Claude Bernard and Wilfred Trotter for a discussion of this important differentiation.

2. It must be admitted that a contemporary research physician is required to be a "basic scientist" in his own field and that his work is often just as "basic" as that done in Departments of Biochemistry and Physiology. Indeed, much research in Departments of Medicine is applied physiology. However, when this has been conceded, it needs to be said that it is easier to do trivial work in clinical research than it is in less applied fields, and it is probably true that more inconsequential work passes as clinical research than exists in more "basic" fields. The fully trained research physician or "clinical investigator" occupies an essential position between the practising physician and the "basic scientist". He must have the clinical confidence of the first and the scientific respect of the second, and he will probably continue to provide the linkage between the basic non-medically qualified scientist and the patient.

3. Because of the increasing complexity of instrumentation used in all kinds of research, we will probably see a continual development of group research activity at least in medicine. In this connection one might note that some "basic scientists"—who would regard a single ameba as impossibly complicated—often completely misunderstand the difficulties that beset the "clinical investigator". As "clinical investigators" we should not be much impressed when such scientists—however eminent—speak against the idea of research groups (which they occasionally do).

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